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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/073,596	05/06/1998	RALPH M. STEINMAN	20164000US5	9977

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EXAMINER
EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/02/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/073,596	Steinman et al.
Examiner	**Art Unit**
G.R. Ewoldt	1644

-- *The MAILING DATE of this communication appears on the cover sheet with the correspondence address* --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *1/3/02 and 4/12/02* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *82 and 84-103* is/are pending in the application.

4a) Of the above, claim(s) *82, 85-88, 90, 93, 96, 98, 100, and 102* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *84, 89, 91, 92, 94, 95, 97, 99, 101, and 103* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. The request filed on 1/03/02 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/073,596 is acceptable and a CPA has been established. An action on the CPA follows.

2. Applicant should amend the first line of the specification to include all priority documents, as set forth in Applicant's letter requesting a corrected filing receipt, filed 12/08/98, and include the updated status of all priority documents.

3. Applicant's election with traverse of Group V (Claims 84, 89, 91-92, 94-95, 97, 99, 101, and 103), in Paper No. 21 is acknowledged. The traversal is on the grounds that consideration of the claims of Group I with the claims in Groups II-VI would not place a serious burden on the Examiner because the claims in Groups I-VI do not have a separate classification in the art, do not have a separate status in the art, and do not require a different field of search. In particular, Applicant argues that all the claims are drawn to dendritic cell precursors. Applicant further argues that there are not different kinds of dendritic cells.

These argument are not found persuasive for the following reasons. While the searches of the related inventions may overlap, and provide some relevant art, the fields of search are different and not coextensive, even though some of the inventions might be classified in the same classes or subclasses. Further compositions comprising different components, e.g., different cells, some presenting unrelated antigens, as well as methods employing said compositions, comprise patentably distinct inventions, the searches of which are not coextensive. As such, the instant search has been found not to be coextensive. One method of demonstrating undue burden is to demonstrate that the searches of the claimed inventions are not coextensive; thus, the searches of Groups I-VI are found to pose an undue burden on the Examiner because they are not coextensive.

Regarding Applicant's argument that there exists only a single type of dendritic cell, i.e., "there are not different kinds of dendritic cells," Applicant is referred to Bottomly, K., (1999) which teaches DC1 and DC2 dendritic cells, known to skew the T cell response towards Th1 and Th2, respectively.

Regarding the instant claims drawn to dendritic cell precursors, it is the Examiner's position that the certain

claims, e.g., 82, 85-86, and 96 may actually be drawn to dendritic cell precursors (even though the specification discloses cells that are more likely to be immature dendritic cells). Claim 101, however, clearly cannot be drawn to a dendritic cell precursor as said term is known in the art, because of the recited limitation that the cell of the claim present antigen. Said cell is known in the art to be a mature dendritic cell (see Steinman in *Fundamental Immunology*, 1999). Further, it is also well-known in the art that the culture of dendritic cell precursors in GM-CSF will result in the generation of either immature or mature dendritic cells from said precursors (see Steinman in *Fundamental Immunology*, 1999, or Romani et al., 1994, IDS). As such, Applicant's use of imprecise and inappropriate language creates a certain ambiguity in just what type of cell is being claimed; the restriction is therefore an attempt to separate the different cell types by their recited limitations.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 82, 85-88, 90, 93, 96, 98, 100, and 102 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 84, 89, 91-92, 94-95, 97, 99, 101, and 103 are being acted upon.

5. New corrected drawings must be filed with the changes incorporated therein. See the attached PTO Form-948. Identifying indicia, if provided, should include the title of the invention, inventor's name, and application number, or docket number (if any) if an application number has not been assigned to the application. If this information is provided, it must be placed on the front of each sheet and centered within the top margin. If corrected drawings are required in a Notice of Allowability (PTOL-37), the new drawings MUST be filed within the THREE MONTH shortened statutory period set for reply in the "Notice of Allowability." Extensions of time may NOT be obtained under the provisions of 37 CFR 1.136 for filing the corrected drawings after the mailing of a Notice of Allowability. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

Corrections other than Informalities Noted by Draftsperson on form PTO-948. All changes to the drawings, other than informalities noted by the Draftsperson, MUST be made in the same manner as above except that, normally, a highlighted (preferably red ink) sketch of the changes to be incorporated into the new drawings MUST be approved by the examiner before the application will be allowed. No changes will be permitted to be made, other than correction of informalities, unless the examiner has approved the proposed changes.

Timing of Corrections. Note that the filing of corrected drawings may no longer be held in abeyance until such time as claims are found allowable. Applicant is required to submit acceptable corrected drawings within the time period set in the Office action. See 37 CFR 1.85(a). Failure to take corrective action within the set period will result in ABANDONMENT of the application.

6. All previous rejections have been withdrawn, thus rendering Applicant's Remarks, filed 1/03/02 moot.

7. The following are new grounds for rejection.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 84, 89, 91-92, 94-95, 97, 99, 101, and 103 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) Claims 84, 89, 91-92, 94-95, and 101 recite "dendritic cell precursors," however, the limitation that the cells "process and present said antigen," recites a property of mature dendritic cells and not dendritic cell precursors (monocytes or $CD34^+$ stem cells), thus, the claims are vague and ambiguous as they recite impossible limitations.

B) Claims 84, 89, 91-92, 94-95, 97, 99, 101, and 103 recite "antigen-activated" "dendritic cell precursors," however, dendritic cell precursors (monocytes or $CD34^+$ stem cells) are not known to phagocytose antigen, thus they cannot be "antigen-activated." As such, the claims are vague and ambiguous as they recite impossible limitations.

C) Claims 91 and 92 are indefinite as they depend on canceled Claim 83.

D) Claims 97, 99, and 103 are indefinite as they depend on non-elected Claim 96.

E) Claim 95 is vague and indefinite in the recitation of "the mycotuberculosis bacteria is BCG," as BCG is *Mycobacterium bovis* bacillus Calmette-Guerin which is not a mycotuberculosis bacteria.

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claim 99 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of "wherein the antigen-activated dendritic cells express an amount of modified antigen to provide between about 1 to 100 micrograms of modified antigen in said pharmaceutical composition."

Applicant's amendment, filed 12/08/98, asserts that support for the claim can be found in original Claims 43-45 and 54-57. However, the claims cannot support the newly added limitations.

12. As set forth in paragraph 2 above, it is unclear just what the claimed composition encompasses. While the claims recite "dendritic cell precursors", the limitations recite properties known to define mature dendritic cells, i.e., antigen presentation. Further, it is well-known that culturing dendritic cell precursors in GM-CSF will result in the maturation of said cells into dendritic cells (see, Inaba et al., 1992, IDS). Therefore, for art purposes, the claimed invention is considered to consist of dendritic cells.

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 89, 91-92, 94-95, 97, 99, 101, and 103 are rejected under 35 U.S.C. 103(a) as being unpatentable over Inaba et al. (1990, IDS) in view of Aldovini et al. (1991).

Inaba et al. teaches dendritic cells pulsed with polypeptide or peptide antigens (see particularly Table 1) that process and present antigen (Table 6, as demonstrated by the cell's ability to prime T cells). The reference further teaches that said pulsed dendritic cells could be useful in "a new approach to immunization" because of their natural adjuvant properties and because the dendritic cell would naturally select the antigen that could be presented on any particular MHC (see page 639, last paragraph).

The reference differs from the claimed invention in that it does not teach the use of a mycotuberculosis, specifically BCG, antigen.

Aldovini et al. teaches that BCG is a well-known mycobacterium antigen used in over two billion tuberculosis immunizations (as of 1991) (see particularly Abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce antigen pulsed dendritic cells that process and present antigen, as said pulsed dendritic cells could be useful for immunization because of their natural adjuvant properties and because the dendritic cell would naturally select the antigen that could be presented on any particular MHC, as taught by Inaba et al., substituting BCG as the antigen of choice, as taught by Aldovini et al. One of ordinary skill in the art at the time the invention was made would have been motivated to make said substitution because BCG is a well-known mycobacterium antigen used in over two billion tuberculosis immunizations, as taught by Aldovini et al., to produce an improved pharmaceutical composition. Note that the references do not specifically teach a pharmaceutical composition, however, it is clear that the Inaba et al. reference envisions pharmaceutical compositions as the

reference discusses the use of dendritic cells in "a new approach to immunization." Further note that the references do not teach the dosage limitations of claims 99 and 103, however, the routine optimization of dosages falls well within the purview of one of ordinary skill in the art and thus lends no patentable weight to the claimed invention.

15. Claim 84 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Inaba et al. (1990, IDS) in view of Aldovini et al. (1991), as applied to claims 89, 91-92, 94-95, 97, 99, 101, and 103 above, and in further view of Caux et al. (1990, IDS) as evidenced by Romani et al. (1994, IDS).

Inaba et al. and Aldovini et al. have been discussed, supra. The references differ from the claimed invention in that they do not additionally teach human dendritic cells.

Caux et al. teaches human dendritic cell precursors ($CD34^+$ stem cells) cultured with GM-CSF and TNFα (see particularly page 2295, column 1, paragraph 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to produce antigen pulsed dendritic cells that process and present antigen, as said pulsed dendritic cells could be useful for immunization because of their natural adjuvant properties and because the dendritic cell would naturally select the antigen that could be presented on any particular MHC, as taught by Inaba et al., substituting BCG as the antigen of choice, as taught by Aldovini et al. and using a human dendritic cell, as taught by Caux et al. One of ordinary skill in the art at the time the invention was made would have been motivated to make said substitutions because BCG is a well-known mycobacterium antigen used in over two billion tuberculosis immunizations, as taught by Aldovini et al., to produce an improved pharmaceutical composition, and to use human dendritic cells, as taught by Caux et al., given that it is most likely that the mouse cells of the Inaba et al. reference were used as models for human cells, particularly in view of Inaba et al.'s discussion of improved immunization, which is unlikely to be meant for mice. Note that the Romani et al. reference merely teaches that the culture of $CD34^+$ stem cells in GM-CSF and TNFα will result in dendritic cell products.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday from 8:00 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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June 28, 2002